



6 October 2015

Dear Shareholder,

You would be aware that Biotron Limited ('Biotron') has recently announced interim data from a key trial of the Company's lead compound BIT225.

The phase 2 trial was a complex three month (12 weeks) dosing study involving 60 patients infected with Hepatitis C virus (HCV) genotypes 1 or 3 at several sites in Thailand.

Two different groups of patients were treated in this trial - those infected with HCV genotype 1 and those infected with HCV genotype 3.

At this time we only have data for the HCV genotype 3 patients as they have a shorter treatment period with IFN/RBV than the HCV genotype 1 patients (24 v 48 weeks). This is dictated by standard treatment guidelines for these drugs.

Genotype 1 results are due during the 1Q16.

We have received many queries from shareholders about the genotype 3 interim data which has been announced. These questions broadly covered three areas:

- The relevance of the excellent result of BIT225 given the performance of the placebo arm.
- The impact of withdrawals on results.
- Where do we go from here?

It is important to understand that **ALL** patients received IFN/RBV – the current standard of care treatment for HCV that can be afforded by most patients. In such a trial, it is expected, hoped, that patients, including those on the placebo combination, will have a beneficial therapeutic outcome.

The primary objective with this study was to assess safety and tolerability of repeat dosing of BIT225 over three months. **We have successfully achieved this.**

The interim data also shows that 88% of patients with HCV genotype 3 treated with BIT225/IFN/RBV had a sustained virological response (SVR) 12 weeks post treatment (SVR12). **This is considered predictive of permanent virus clearance – i.e. cure.**

In the placebo group, 90% of patients also had SVR12. These results are somewhat surprising given that, historically, only around 68% of patients would have an SVR at 12 weeks with IFN/RBV. However, response rates to IFN/RBV can vary, depending on many factors, including age, gender, genetics, degree of liver damage, amount of virus in the system and others.

The reality is that both cohorts had an outstanding response. BIT225 has not failed in this trial. It is just that IFN/RBV was unexpectedly effective in treating this particular set of patients.

The BIT225 group was adversely impacted because 12 out of 20 patients withdrew from the study for reasons beyond our control and **in most cases NOT because of ill-effects from BIT225**. It is known that HCV patients can suffer a broad range of adverse side effects from IFN/RBV and under well-established, international clinical trial regulations, we were not able to replace these trial subjects with other candidates.

SVR12 results from the genotype 1 cohort of the trial are due during the 1Q16. We are also optimistic of a positive outcome for this group. While efficacy data are unavailable now because patients are still receiving IFN/RBV, we note there have been far fewer withdrawals from the study in this set of 30 patients.

Finally these results must also be considered in a market context. There remains a real need for new classes of drugs to treat Hepatitis C. More patients than anticipated are failing treatment with some of the new HCV drugs and there have been signs of development of drug resistance. BIT225 continues to demonstrate it is a highly promising drug candidate for this market. Nothing has changed.

To summarise, Biotron's clinical development program for BIT225 has:

- Demonstrated further safety, tolerability over a 3 month dosing period.
- Generated a comprehensive pharmacokinetic data package.
- Proved that the capsule formulation of BIT225 is more effective than previous powder formulations.
- Generated positive BIT225 data from trials in more than 200 subjects.
- Generated important data that will allow us to accurately define BIT225 dose and dose frequency in future studies.

Data from this, and past trials, will now be included in an IND (Investigational New Drug) submission to the USA Food and Drug Administration (FDA) and will also inform a comprehensive data pack being compiled for prospective partners. Future studies will focus on combining BIT225 with new classes of HCV drugs.

Your Company's Directors continue to believe that it has a strong drug candidate in BIT225 for both HIV and HCV and that the Company remains in a competitive commercial position.

I thank you for your ongoing support and look forward to updating you with further study results and positive progress.

Sincerely,



**Dr Michelle Miller
Managing Director**